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¹ Gregory, John
² Berlin, Robert A.



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ON THE USE OF CODEINE TO RELIEVE PAIN IN ABDOMINAL DISEASE.

BY T. LAUDER BRUNTON, M.D., F.R.S.

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I HAD intended to bring the subject of this paper before the British Medical Association at its last meeting, but I was unfortunately prevented from attending, and delayed publication of this paper for several reasons, one of which was the desire to obtain a larger experience of the utility of the drug. The relief of pain may be classed next to the saving of life, and must perhaps sometimes be even put before it as the chief duty of the physician. As yet no drug has taken the place of opium as a general analgesic, though the use of crude opium is now frequently replaced by the subcutaneous injection of morphine, the most active of the alkaloids it contains. In abdominal pain many practitioners still have a preference for the use of opium, as compared with that of morphine, and this very preference is sufficient to make one ask whether it may not have some foundation in the presence of other active principles along with morphine in opium, and if so, to inquire which active principle it is that helps to allay pain.

Thanks to its recommendation by Dr. Pavy, codeine is largely used in the treatment of cases of diabetes, but at present its use is almost confined to this disease, and it is rarely employed for other purposes, excepting perhaps that of soothing cough or irritation in the throat.

Codeine was discovered by Robiquet in 1832, and two years afterwards its action was tested upon himself by Gregory,¹ who found that instead of causing sleep, it rather caused excitement, and had also a slight laxative tendency. It was applied therapeutically by Barbier² in 1834, who noticed that it seemed to have a special action upon the sympathetic system, and found that it was of great use in lessening pain in persons presenting symptoms of irritation in the solar plexus. Such symptoms are pain in the epigastrium, spreading to the sides and back, and associated with a feeling of burning, anxiety, depression, more or less tenderness of the epigastrium, with sighing, lack of energy and tendency to faint. Occasionally the pain may cause symptoms of collapse, palpitation, and vomiting. In such cases Barbier gave a grain of codeine in a tablespoonful of syrup, and repeated it if necessary in one or two hours with the best results. From his observations he came to the conclusion that codeine

¹ Gregory, *Journ. de Pharm.*, February, 1834.

² Barbier, letter to Acad. de Méd., *Schmidt's Jahrb.*, vol. ii, p. 267.

acts chiefly upon the sympathetic nervous system, and especially upon that part of it which is in the region of the stomach; that it is a most useful remedy in abdominal neuroses depending upon disordered condition of the nervous plexus in the abdomen, and especially those in the gastric region; that it does not disorder the digestion, and rather aids than interferes with the action of the bowels. He found also that it produced sleep with tolerable certainty, and that this sleep was never followed by heaviness in the head or stupidity, but, on the contrary, persons who had taken it felt happy, and were disposed to be cheerful on awaking. About twenty years later, in 1856, Robiquet's³ son undertook some observations on the action of the drug which his father had discovered. The results he obtained, however, did not quite accord with those of Gregory or of Barbier, and it is possible that the discrepancies may have been due to more or less impurity in the drug employed. In large doses he found that it caused an unrefreshing sleep, followed by a period of confusion of thought; occasionally nausea and vomiting were produced. In small doses he found it of great service in hypochondriasis, relieving nervousness, irritability, and all the discomforts from which patients affected with this disorder are apt to suffer.

Shortly afterwards Berthé⁴ made a much more full and complete investigation of the physiological action of the alkaloid. Amongst other things he confirmed Barbier's observation that it had a specific action upon the sympathetic, and found that it lessened the irritability of the intestine to such an extent that a dog which had received 15 grains of arsenic along with $7\frac{1}{2}$ grains of codeine exhibited neither vomiting nor purging, nor any other symptom excepting drowsiness, while another dog which had received a similar dose of arsenic without the codeine began to suffer in the course of an hour from severe pain, vomiting, and bloody diarrhoea, and indeed presented well-marked symptoms of arsenical poisoning, although it ultimately recovered. These experiments suggested the idea to me that codeine was likely to be of service in abdominal pain, and I proceeded to try it, with very satisfactory results. The class of cases in which I have used it is, I think, somewhat different from those in which it has previously been recommended, because while Barbier, Aran and others have chiefly employed it in gastralgia and painful disorders of the stomach, I have used it chiefly in pain affecting the intestine and lower part of the abdomen. The kinds of cases in which I have used it have been very varied. As examples I may shortly describe one or two. In one case which I saw with Dr. Eccles, there was high temperature, intense pain in the right iliac fossa, with considerable swelling, so that there could be little doubt that there was inflammation around the cæcum, although examination after the acute symptoms had subsided showed that there was also pelvic cellulitis. In this case one grain of codeine, given in the form of a pill, relieved the pain at once, and repetition of the dose whenever the pain began to return prevented its becoming at all severe.

In another case, seen with Dr. Philpot, of Croydon, a lady, aged 50, had pneumonia of the right base, a greatly dilated heart with very irregular action, pulse so rapid and weak that it could hardly be counted, and pain over the epigastrium and spreading out from it. She was slightly jaundiced, and a tumour was felt in the right lateral abdominal region, which descended with respiration, but was partly covered by intestine, and could be moved from side to side, so that it seemed to be renal rather than hepatic. As no

³ Robiquet, *Gaz. des Hôp.*, 1856, xxix, 517.

⁴ Berthé, *Moniteur des Hôp.*, 1856, iv, 596, 601, 692, 1052.

post-mortem examination was obtained the exact diagnosis could not be established, but the administration of codeine in half-grain doses relieved the pain, as Dr. Philpot said, "as if by magic."

In another case, seen with Dr. Pardington at Tunbridge Wells, there was pain in the abdomen depending upon a mass of impacted faeces in the transverse colon. In this case codeine seemed to be especially indicated, as one wished to relieve the pain without interfering with the action of the bowels. In grain doses codeine relieved the pain, and the use of copious enemata, aided by washing out the stomach, cleared away the impacted mass which had given rise to the disturbance. I have tried codeine in cases of long-continued abdominal pain for which no definite cause could be assigned, as no tumour could be felt, and the functional disturbance did not seem sufficient to warrant a diagnosis of malignant disease. I have tried it in cancer of the liver and pancreas with success in relieving pain, and also in numerous cases where the age of the patient, the presence of diarrhoea, tenderness on pressure, and visible peristaltic movements, and thickening of the gut, easily perceptible on palpation, led to the diagnosis of malignant disease in the intestine, although inability to obtain a *post-mortem* examination prevented the confirmation of the diagnosis. In such cases I generally begin with half a grain, in the form of a pill made up with extract of gentian, three times a day; and if this is insufficient to control the pain I increase the dose to a grain, and give it as frequently as seems necessary. As a rule, I find that it does not produce drowsiness, nor has it interfered with the digestive functions.

To sum up, the results I have obtained from the administration of codeine have satisfied me that it has a powerful action in allaying abdominal pain, and it can be pushed to a much greater extent than morphine without causing drowsiness or interfering with the respiration or with the action of the bowels. It is, therefore, specially indicated in such a case as Dr. Philpot's, which I have already mentioned, where the dilated heart and consolidated lung tended to make one afraid of morphine. Codeine is also specially indicated in a case like Dr. Pardington's, where one wished to relieve the pain without interfering with the action of the bowels. On the other hand, in cases where there has been much diarrhoea, as in some cases of malignant disease of the colon or rectum, the absence of any tendency to lessen peristaltic movement is rather a disadvantage to codeine as compared with morphine or opium.

I have found that in cases of long-continued enteralgia without organic disease, it has continued to relieve pain for months together, without the dose being increased beyond one grain three times a day, and I found the same to be the case where the presence of a tumour, in addition to other symptoms, had led to the diagnoses of malignant disease.

It is interesting to follow the vicissitudes of a drug, and to notice how its use extends or diminishes until at last it finds its right place and maintains it. Thus digitalis, while mentioned in the London *Pharmacopœia* of 1721, was excluded from that of 1746. It again appeared in 1788, and since then it has held its place.

Possibly codeine, after falling into almost complete disuse as an analgesic for many years may again regain a more or less important place amongst the remedies which enable us to relieve pain.



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